REMARKS

This is a response to the Office Action mailed August 15, 2003. Claims 1-3, 5-7, 10-32, 37-39, 41-44 and 46-85 are pending in the application. Claims 1-3, 5-7, 10-32, 37-39, 41-44 and 46-72 have been rejected by the Examiner. As noted above, Applicants have amended Claims 1, 2, 6, 13-16, 18, 20-26, 31, 32, 37, 41, 42, 65, 69 and 70, and added Claims 73-85. The amendments and new claims are fully supported by the written description. Also, no new matter has been introduced into the application.

Claim Rejections – 35 U.S.C. § 102

A. Crocker et al.—Claims 1, 2, 6, 7, 10-16 and 37-39

The Examiner has rejected Claims 1, 2, 6, 7, 10-16 and 37-39 under 35 U.S.C. §102(b) as being anticipated by Crocker et al. (U.S. Patent No. 5,782,742). Crocker et al. is directed to a balloon catheter having an inflatable balloon with a radiation carrier such as a radiation delivery layer (see abstract). Crocker et al. disclose a radioactive balloon that "comprises a proximal zone 28, and a distal zone 30 having approximately equivalent inflated diameters. The proximal zone 28 and distal zone 30 are separated by an enlarged central zone 32" (col. 6, lines 19-23). Crocker et al. further disclose that "[e]nlarged zone 32 is provided with a radiation source 34, preferably **distributed uniformly throughout the circumference of the balloon**" (col. 6, lines 24-26) (emphasis added).

According to the Federal Circuit, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631 (Fed. Cir. 1987). Crocker et al. clearly fail to disclose all of the limitations of the claimed invention. Crocker et al., for instance, do not disclose all of the limitations of amended Claim 1, such as "an elongated source of a therapeutic agent, **the source having a concentration of the therapeutic agent that**

gradually changes along a length of the elongated source near a proximal end or a distal end of the elongated source." Crocker et al. also do not disclose all of the claimed limitations of amended Claims 6, 13, and 37. For example, Crocket et al. do not disclose an elongated radiation delivery source that includes a radioactive region wherein "the radioactive region includes **a segment gradually transitioning from the therapeutic level to a non-therapeutic level of radioactivity near the proximal end or the distal end of the radioactive region**" as recited by amended Claim 6.

Crocker et al. specifically do not disclose that the concentration of radiation gradually changes along the length of the balloon. Referring to Figure 4 of Crocker et al., a copy of which is attached hereto at Exhibit A, the Crocker et al. balloon has a proximal zone 28, a distal zone 30, and a central section 32. Radiation source 34 is only disclosed along central section 32. There is nothing in Crocker et al. that suggests radiation source 34 includes radioactivity that gradually changes along the length of radiation source 34.

Crocker et al. recognize the problem of delivering a non-uniform radiation dose about the circumference of the balloon (see col. 2, lines 1-6; "delivery of a uniform dose of radiation circumferentially around the artery is difficult with the radioactive guidewire-type delivery systems, unless the guidewire is centered within the artery such as through the use of a balloon catheter.") Crocker et al., however, are silent regarding the dose profile along the length of radiation source 34, suggesting that the level of radioactivity would be constant along the length. The Crocker et al. balloon, therefore, would have a radioactivity profile that corresponds to the "typical" radiation dose profile that was known before the filing of the current application. As illustrated from Exhibit B[1], the "typical" radioactivity dose profile includes a sharp transition from the radioactive region to the absence of radioactivity. Because radiation source 34 of

[1] Exhibit B is adapted from Figure 3 of the current application.

Crocker et al. is only applied along central section 32, the radioactivity profile would only extend along a part of the length of balloon 18 and then have a sharp transition to an absence of radiation. In Exhibit B, the sharp transition of radioactivity is indicated by the lines labeled A and B.

Crocker et al.'s radioactivity profile is in stark contrast with the elongated source of Claim 1 which has a gradual change along the length of the source. Representative examples of profiles that have a gradual change in activity are illustrated in Figures 4, 5 and 6 of the application as filed. Comparing Exhibit B with Figures 4, 5, and 6 certainly shows that the Crocker et al. concentration profile is different than the claimed invention.

Additionally, with respect to independent Claim 37, Crocker et al. do not disclose a method of producing a **drug source**, including "forming a **drug region on a drug source**." Crocker et al, instead, is limited to a radiation balloon capable of delivering therapeutic radiation. One of ordinary skill in the art clearly understands that "radioactivity" is not equivalent to a "drug compound." The distinction between these two types of therapeutic agents is clearly set-forth throughout the present application, for example in at least paragraphs 23 and 50-66. Nowhere in Crocker et al. is it suggested that the catheter balloon is capable of delivering a **drug** such as anti-inflammatory compounds, anti-proliferative compounds, anti-migratory compounds, inhibitors of matrix or collagen deposition, or apoptosis inducers.

Accordingly, independent Claims 1, 6, 13, and 37 are allowable over Crocker et al. Dependent Claims 2, 7, 10-12, 14-16, 38 and 39 should also be allowable.

B. Turnlund et al.—Claims 21-32, 46-48, 50-55, 57-60, 62, 63 and 65-67

The Examiner has rejected Claims 21-32, 46-48, 50-55, 57-60, 62, 63 and 65-67 under 35 U.S.C. §102(e) as being anticipated by Turnlund et al. (US 2001/0001806A1). Turnlund et al. is directed to a method for increasing the rate of thrombus formation and/or proliferative cell growth of a selected region of cellular tissue by endovascularly irradiating the selected region

with radiation (see abstract). According to Turnlund et al., "[p]referably, the delivery means includes a deformable endovascular prosthesis (25) adapted for secured positioning adjacent to the selected region (21) of cellular tissue (22), and a radioactive source" (abstract). Turnlund et al. disclose that a stent graft can be "constructed to deliver a dose of endovascular radiation upon the selected region 21 (i.e., the arterial wall of the aneurysmal sac 27 that is formed between the stent graft and the wall of the blood vessel), while maintaining vessel patency" (page 4, paragraph 40). Turnlund et al. further disclose that "to limit potentially occlusive in-growth at the proximal and distal ends of stent graft 23, the proximal and distal end portions of the stent which anchor the stent to the vessel may have different activities as compared to the growth inducing radioactivity of the central portion 38 of the stent (FIG. 8)" (page 6, paragraph 57).

It is the Examiner's position that Turnlund et al. anticipate Claims 21-32, 46-48, 50-55, 57-60, 62, 63 and 65-67 because Turnlund et al. "appreciates the radiation dosages should not be as high at the proximal and distal portions" of the stent-graft. The Examiner points to Figure 6 and has argued that Figure 6 shows that the dose along the length of the stent-graft decreases "from the central region (38) toward an end of the stent, thus, displaying the stent is configured to irradiate different levels of radiation longitudinally along the stent." Although Turnlund et al. disclose a stent with proximal and distal end portions that can have "**different activities**" as compared to the central portion of the stent, Turnlund et al. absolutely do not disclose a stent that has **a concentration of a therapeutic agent that gradually changes along the length of the stent**. For instance, Turnlund et al. fail to disclose a stent including a radioactive region along a length of a stent, where the stent includes "a radioactivity gradient near a proximal end or a distal end of the radioactive region, **the radioactivity gradient gradually decreasing the dose delivered to the vessel from a therapeutic level to a non-therapeutic level of radioactivity**" as recited by Claim 21. Nor does Turnlund et al. disclose a stent having drug concentration gradients where the "a concentration gradient [is] **gradually decreasing** from a therapeutic dose

level to a non-therapeutic dose level" as recited by Claim 31. Moreover, Turnlund et al. do not disclose a stent having a therapeutic agent deposited on a body of the stent, where "**the concentration or amount of therapeutic agent gradually changes along a length of the stent,**" as recited in Claim 46; or a method of making such a stent, as claimed in Claim 53.

In contrast to a stent that has a concentration of a therapeutic agent that **gradually changes** along the length of the stent, Turnlund et al. discloses a stent-graft having a radioactivity dose profile that includes a sharp transition from the radioactive region to the absence of radioactivity. Referring to Figure 6 of Turnlund et al., which is attached as Exhibit C, the dose profile of the Turnlund et al. stent shows that there are sharp peaks of radioactive dose at 0.1 mm out from the stent surface. Because Figure 6 shows a general trend of a more uniform radioactivity dose at farther distances from the stent-graft surface, one can deduce that the radioactivity profile of the Turnlund et al. stent would have sharp peaks along the length of the stent-graft. The sharp transitions from high radioactivity to no radioactivity along the length of the Turnlund et al. stent-graft is clearly different than a "gradual" transition or change of the current application.

Additionally, with respect to independent Claims 31, 63, 65 and 67, Turnlund et al. do not disclose a stent having a **drug gradient** along a length of the stent. Although Turnlund et al. suggests that the stent-graft can be used in combination with proteins or gene therapy (see, e.g., paragraphs 51 and 71), there is nothing in Turnlund et al. to suggest that any drug would have a concentration gradient along a length of the stent-graft. Turnlund et al, instead, only suggest that "the proximal and distal portions of the stent which anchor the stent to the vessel may have different activities as compared to the growth inducing **radioactivity** of the central portion 38 of the stent" (paragraph 57 on page 6) (emphasis added). As noted above, one of ordinary skill in the art clearly understands that "radioactivity" is not equivalent to a "drug compound." Nowhere in Turnlund et al. is it suggested that there is a drug gradient for drug compounds such as anti-

inflammatory compounds, anti-proliferative compounds, anti-migratory compounds, inhibitors of matrix or collagen deposition, or apoptosis inducers.

Applicants again respectfully request the Examiner to reconsider the Section 102(e) rejection and allow Claims 21-32, 46-48, 50-55, 57-60, 62, 63 and 65-67.

Claim Rejections – 35 U.S.C. § 103

A. Crocker et al. in view of Turnlund et al.—Claims 3 and 5

The Examiner has rejected Claims 3 and 5 under 35 U.S.C. §103(a) as being unpatentable over Crocker et al. in view of Turnlund et al. As noted above, Claim 1 is allowable over Crocker et al. The disclosure of Turnlund et al. does not cure the deficiencies of the prior art reference as related to Claim 1. Accordingly, Claim 1 is allowable over Crocker et al. in view of Turnlund et al. Claims 3 and 5 depend directly from Claim 1, and are allowable for at least the same reason.

B. Crocker et al. in view of Tang et al.—Claims 17, 18, 49, 56, 61, 64, 68 and 69-72

The Examiner has rejected Claims 17, 18, 49, 56, 61, 64, 68 and 69 under 35 U.S.C. §103(a) as being unpatentable over Crocker et al. in view of Tang et al. (U.S. Patent No. 6,524,232[2]). Effective November 29, 1999, subject matter which was prior art under former 35 U.S.C. §103 via 35 U.S.C. §102(e) is now disqualified as prior art against the claimed invention if that subject matter and the claimed invention, "were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person" (see MPEP Section 706.02(l)(1)). A statement of an attorney of record can be sufficient evidence to establish common ownership (see MPEP Section 706.02(l)(2)).

As established by the enclosed Statement of Common Ownership, at the time the invention of the current application was made, the inventions of the current application and Tang

[2] In the Office Action mailed August 15, 2003, the Examiner notes on page 5 that the Tang et al. reference has the U.S. Patent No. of 6,504,232. It appears that the patent number on page 5 was a typographical error, and should be 6,524,232, which is the number listed in the Notice of References Cited attached to the Office Action.

et al. (U.S. Patent No. 6,524,232) were owned by, or subject to an obligation of assignment to, Advanced Cardiovascular Systems, Inc., a California corporation. Since the Applicants have established common ownership, Tang et al. is disqualified as prior art and should be removed as a reference. Accordingly, Claims 17, 18, 49, 56, 61, 64, 68 and 69 are allowable. Applicants respectfully request withdrawal of the rejection and allowance of the claims.

C. Crocker et al. in view of Malik et al.—Claims 19, 20, 49, 56, 61, 64, 68 and 69-72

The Examiner has rejected Claims 19, 20, 49, 56, 61, 64, 68 and 69-72 under 35 U.S.C. §103(a) as being unpatentable over Crocker et al. in view of Malik et al. (U.S. Patent No. 6,504,307). As established by the enclosed Statement of Common Ownership, at the time the invention of the current application was made, the inventions of the current application and Malik et al (U.S. Patent No. 6,504,307) were owned by, or subject to an obligation of assignment to, Advanced Cardiovascular Systems, Inc., a California corporation. Since the Applicants have established common ownership, Malik et al. is disqualified as prior art and should be removed as a reference. Accordingly, Claims 19, 20, 49, 56, 61, 64, 68 and 69-72 are allowable. Applicants respectfully request withdrawal of the rejection and allowance of the claims.

D. Crocker et al. in view of Segal—Claims 41-44, 49, 56, 61, 64 and 68

The Examiner has rejected Claims 41-44, 49, 56, 61, 64 and 68 under 35 U.S.C. §103(a) as being unpatentable over Crocker et al. in view of Segal (U.S. Patent No. 6,059,752). Segal is directed to a mechanical dilation and irradiation device for enlarging a flow passage of a vessel by dilating and irradiating an obstruction in the vessel (see abstract).

To establish *prima facie* obviousness, **all of the claimed limitations** must be taught or suggested in the references cited. In re Royka, 490 F.2d 981 (CCPA 1974). Crocker et al. and Segal, alone or in combination, fail to teach or suggest all of the limitations of the claimed invention. Neither Crocker et al. nor Segal disclose an implantable medical device that has a

concentration of a therapeutic agent that gradually changes along the length of the device. As noted above, Crocker et al. merely disclose a radiation source 34 disposed along central section 32 of balloon 18, providing a "typical" radioactivity dose profile that includes a sharp transition from the radioactive region to the absence of radioactivity. The disclosure of Segal does not cure this deficiency of the Crocker et al. reference. Segal merely discloses that a contractible material can be applied over a radiation delivery source. There is no mention in Segal of applying the contractible material to the source so that the radiation level gradually changes along the length the device. Instead, Segal merely suggests that the contractible material can be used "to protect the vessel wall from damage and prevents potential entrapment of tissue between the flexible elongate elements 36 as they are being compressed axially while still permitting the relative free passage of blood into proximal extremity 87 and into the central flow passage 89 and out distal extremity 89" (col. 12, lines 3-10).

Additionally, with respect to Claims 49, 56, 61, 64, and 68, neither Crocker et al. nor Segal suggest an implantable medical device having a therapeutic agent deposited within a polymeric coating. Segal, for instance, merely discloses an expansion member that "is covered or encapsulated with a radially expandable and contractible material 91 such as a latex, polyurethane, silicone or other thermoplastic elastomer" (col. 11, lines 46-48). Although Segal suggests that such a coating could be formed by (1) masking off a part of the device, (2) dipping the expansion member into the desired coating material, and (3) curing the material, there is nothing in Segal that suggests that the described process would include incorporating a therapeutic agent such as a drug compound into the coating material before the material is applied to the expansion member. In short, Segal clearly does not disclose that the contractible material could have any therapeutic agent. Instead, the contractible material was merely meant by Segal to provide protection of the vessel during the device's deployment.

Claims 41-44, 49, 56, 61, 64 and 68 are allowable over the Crocker et al. in view of Segal.

Applicants respectfully request withdrawal of the rejection and allowance of the claims.

CONCLUSION

Claims 1-3, 5-7, 10-32, 37-39, 41-44 and 46-85 are pending in this application. Examination and allowance of the claims are respectfully requested. If the Examiner has any questions or concerns, the Examiner is invited to telephone the undersigned attorney at (415) 954-0345.

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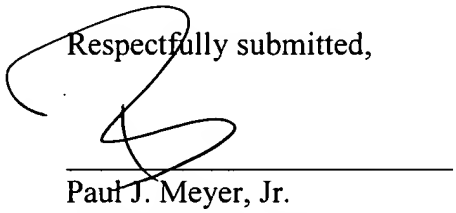
Respectfully submitted,



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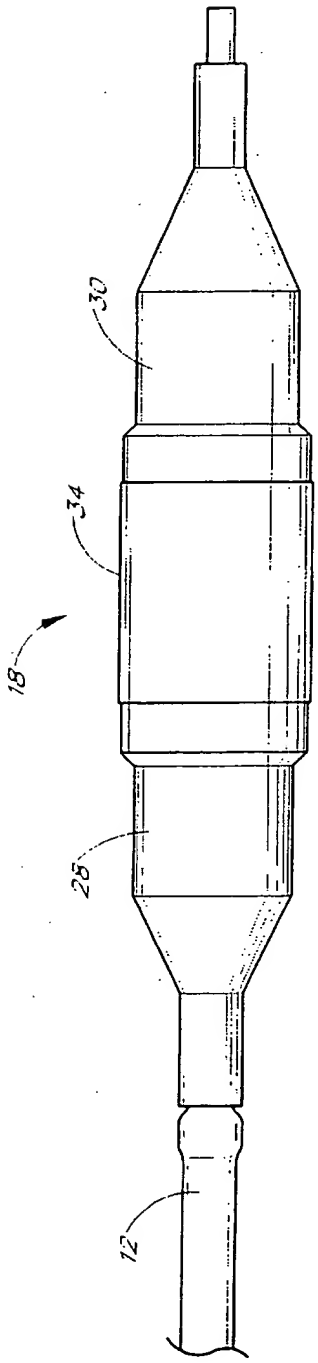


FIG. 3

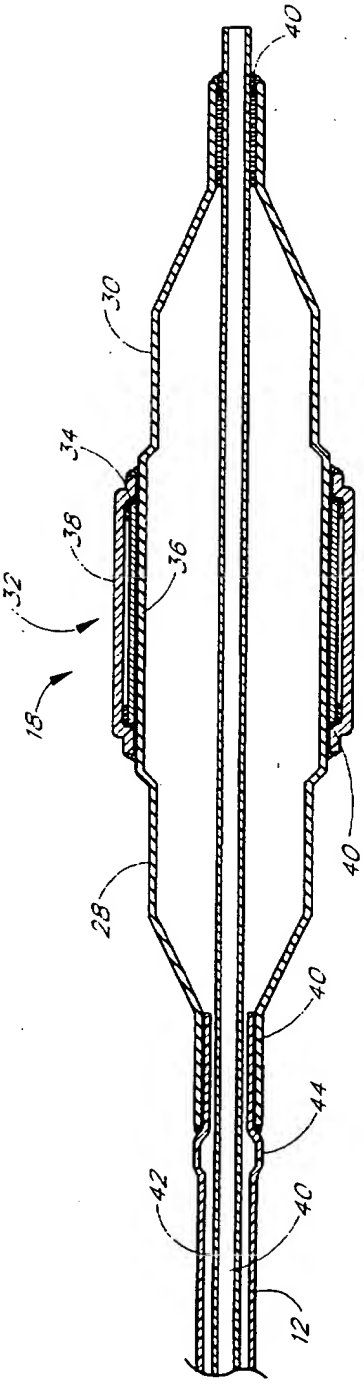
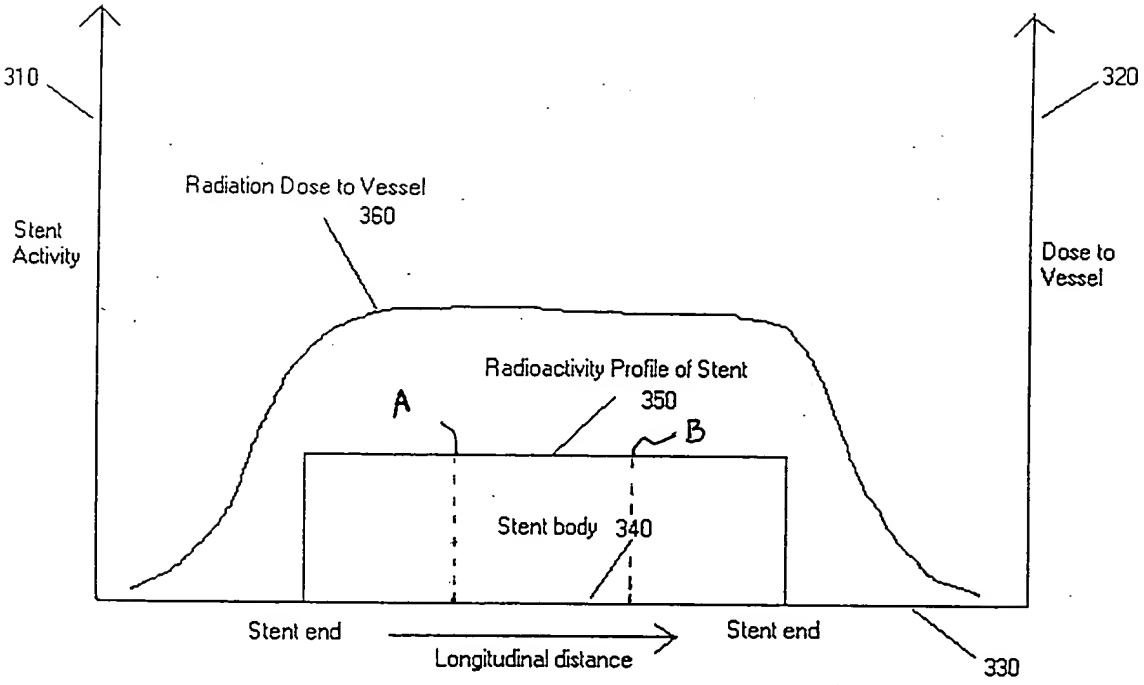


FIG. 4

EXHIBIT A

Exhibit B


310
320
Radiation Dose to Vessel
360
Stent Activity
Dose to Vessel
Radioactivity Profile of Stent
350
A
B
Stent body 340
Stent end
Stent end
Longitudinal distance
330

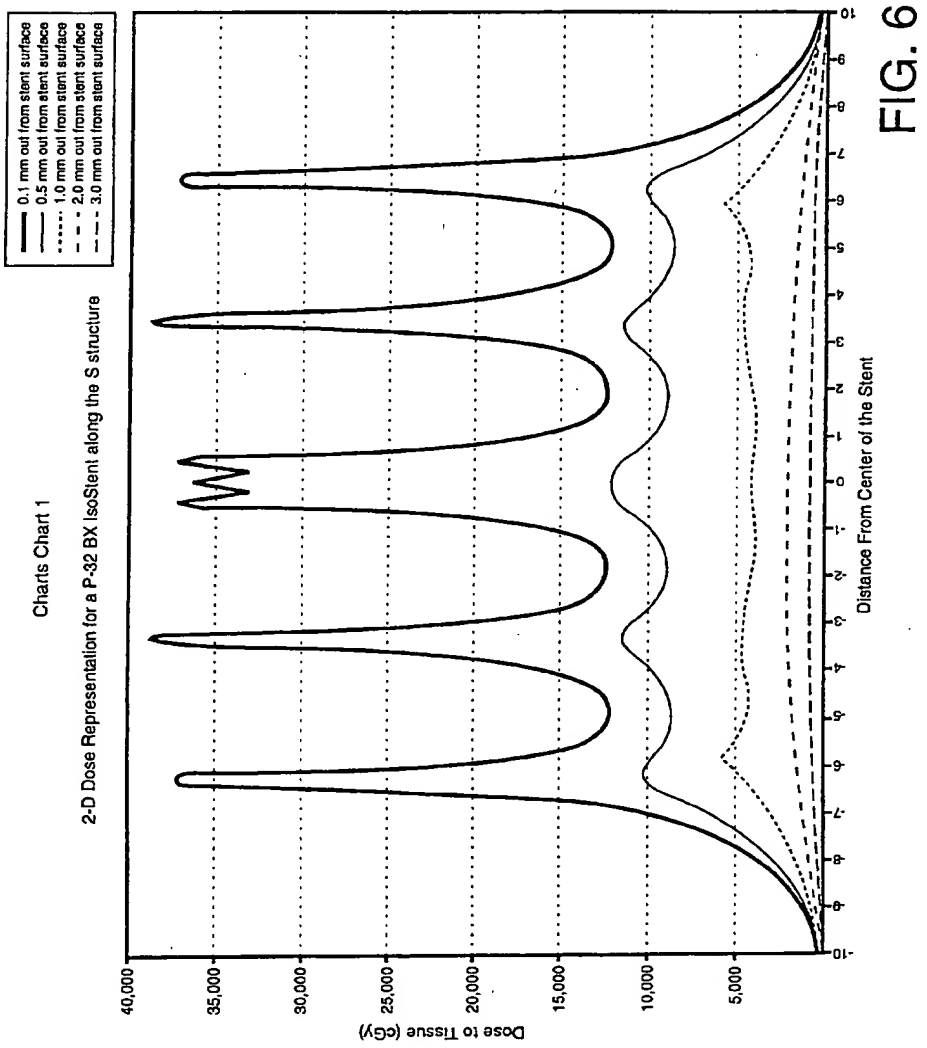


FIG. 6

EXHIBIT C